COMSOL Simulation of a BioMEMS Disease-diagnostic Lab-on-a-Chip Device

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Abstract

Efficient, portable and accurate Disease Diagnostic systems are in great demand for modern clinical testing industry. Such systems are especially needed for patients with complicated health conditions. For example, some patients may have a variety of diseases, conventional testing methods may not be able to check it out all at once. In case of an emergency, failure to accurately determine the cause could be fatal for the patients. In this poster, a complete lab-on-a-chip device for disease diagnosis based on BioMEMS (Bio-Micro-Electro-Mechanical-Systems) technology is proposed. The proposed efficient disease diagnosis system integrates micropump, micromixer and gel electrophoresis component into a single chip. An on-chip control circuitry is used to store the pre-programmed blood sampling, buffering and chemical delivery sequence. Based on the theoretical analysis, a set of optimized design parameters of the lab-on-chip system are suggested. The working principle of the efficient disease diagnostic system is discussed. COMSOL simulation is used to verify the function of the system. The proposed efficient disease diagnostic system offers excellent efficiency, accuracy and portability compared to traditional disease diagnostic procedure. If integrated with other testing chips, it could provide a useful tool for biomedical field and be crucial for micro total analysis system.

Introduction

A lab-on-a-chip (LOC) is a device that integrates one or several laboratory functions on a single chip with size of millimeters to a few square centimeters. LOCs deal with the handling of extremely small fluid volumes down to less than pico-liters. Lab-on-a-chip devices are a subset of MEMS devices and also called as "Micro-Total-Analysis-Systems" (μTAS). LOC is closely related to, and overlaps with, microfluidics which describes primarily the physics, the manipulation and study of minute amounts of fluids. However, strictly speaking, "Lab-on-a-Chip" refers to the scaling of single or multiple lab processes down to chip level, whereas "μTAS" is dedicated to the integration of the total sequence of lab processes to perform chemical analysis. The term "Lab-on-a-Chip" was introduced later on when it turned out that μTAS technologies were more widely applicable than only for analysis purposes.

Lab-on-a-Chip Design

In this poster, a silicon-based printed circuit board lab-on-a-chip is proposed. As shown in Fig. 1, the proposed LOC consists of a piezoelectric micropump, a passive micromixer, a micro electric heater, a silicon photodetector and a gel dielectrophoresis part.

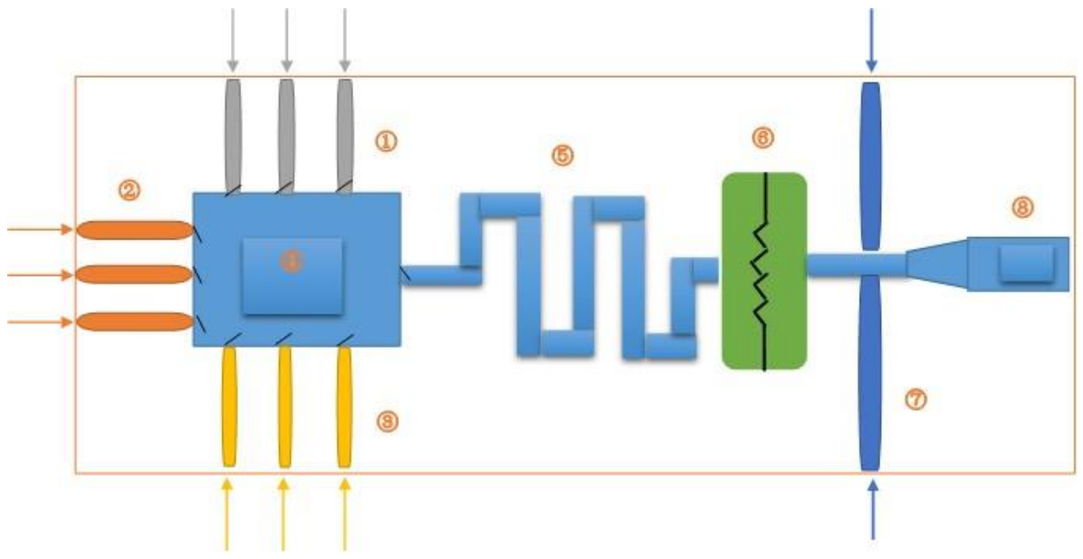


Figure 1: Schematic diagram of Lab-on-a-Chip device for disease diagnosis

In the figure, 1-3: Buffer, dilution, blood sample and reacting solution loading area; 4. piezoelectric micropump; 5. microchannel assembled with passive micromixer, 6. micro thermal resistor; 7. gel dielectrophoresis area; 8. silicon photodetector.

The working principle of the lab-on-a-chip device is explained as below. For disease diagnosis, a tiny drop of blood sample is collected from patient and delivered into loading ports. The micropump then pumps the blood sample into the pump chamber. Since very tiny amount of blood sample is used, the protein or DNA samples in it are very minute. In order for the signal to be strong enough for detection, it is necessary to duplicate the protein or DNA segments in the sample. By adding the Polymerase Chain Reaction (PCR) buffer solution, and heat it up with appropriate thermal cycles, the DNA segments in the sample can be duplicated into large amount very quickly. In the working mode, the micropump is turned on to pump the mixed solution of both blood sample and PCR buffer solution into the micromixer. The micro heater then heats up the solution to 94ºC, so that DNA double helix chains are broken apart. After that, the solution is annealed down to 60ºC to allow single-stranded primers to bind to their complementary single-stranded bases on denaturated DNA. Then the solution is again heated up to 72ºC for the Taq polymerase to attach and start copying the template. This results in two new double helixes in place of the first one. By repeating the above cycle again and again, the DNA samples will be quickly duplicated to meet the test requirement. Then enzyme-linked immunosorbent assay (ELISA) solution is added to dye the specific protein or ribose particle to different colors. Dielectrophoresis is used to drive the dyed particle apart from the main flow. Finally they will gather together to be detected.

COMSOL simulation is used to verify the function of the Lab-on-a-Chip device. The COMSOL model geometry is shown in Figure 2.

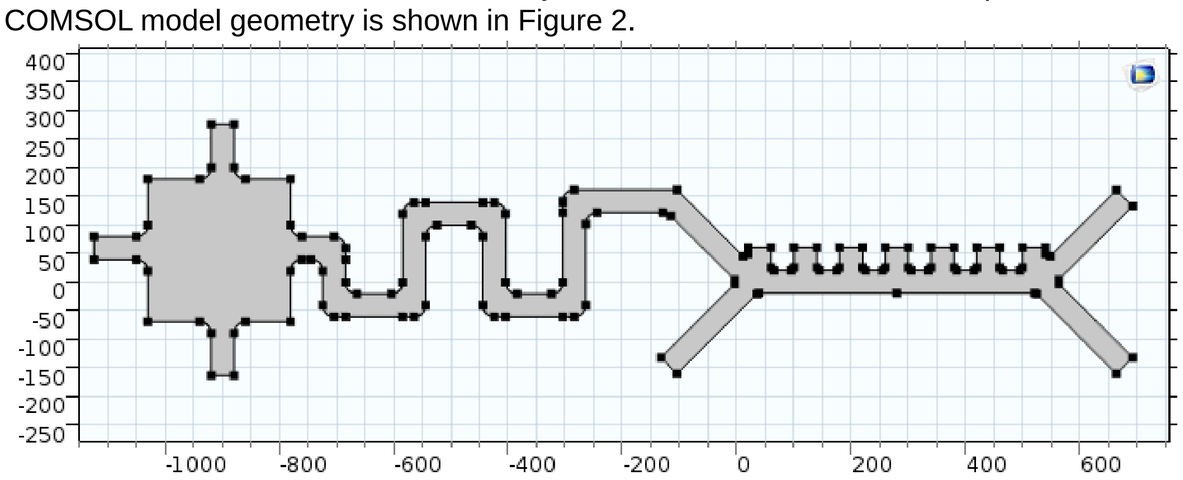


Figure 2: Lab-on-a-Chip design in COMSOL

COMSOL Simulation

COMSOL transient simulation is used to see how quick the blood sample can be mixed with buffer/dilution and chemical solutions along the microchannel. As shown in Figure 3, the blood sample and buffer/dilution, chemical solutions are introduced from inlet ports to micropump. They are mixed well already in the pump, and then flowed into the micromixer, where it would react completely. In Figure 3, water solutions are used for microfluidic flow in COMSOL simulation. If blood sample and PCR solution are used, their viscosities and temperature also need to be considered.

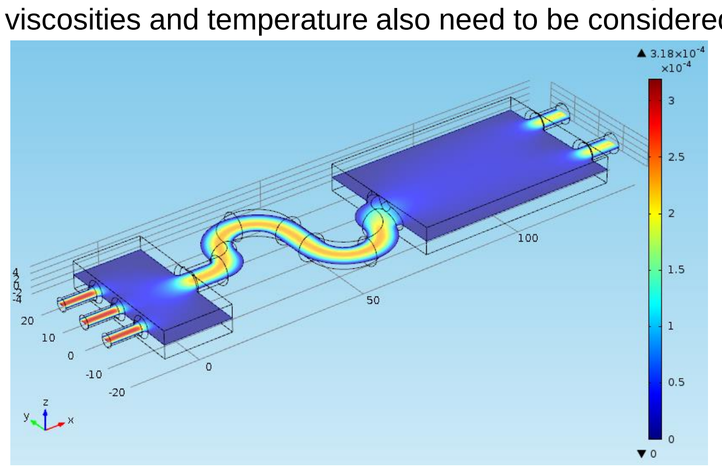


Figure 3: Velocity plot of microfluid in COMSOL simulation of 3D LoC device

The COMSOL simulation result in Figure 3 shows that the dielectrophoresis part can successfully separate different particles with different electric potential. At the end of the outlet, all the particles with same electric potentials are stacked together so that they can be detected by Scanning Electron Microscope. If the sample is pure enough and amount is large enough, it may be even directly seen by human eyes. This would significantly accelerate the diagnosis process to achieve a quick decision on the disease treatment therapy.

After the test sample meets the reaction requirement, the ELISA solution can be added to the chip. After the staining reaction is finished, dielectrophoresis function can be performed for the solution. By adding different electrostatic forces, the particles with different electric potentials can be deviated away from the main flow via different routes, hence they are separated from each other. Figure 4 shows the COMSOL simulation result of particle trajectories of microfluid dielectrophoresis after time t=7sec.

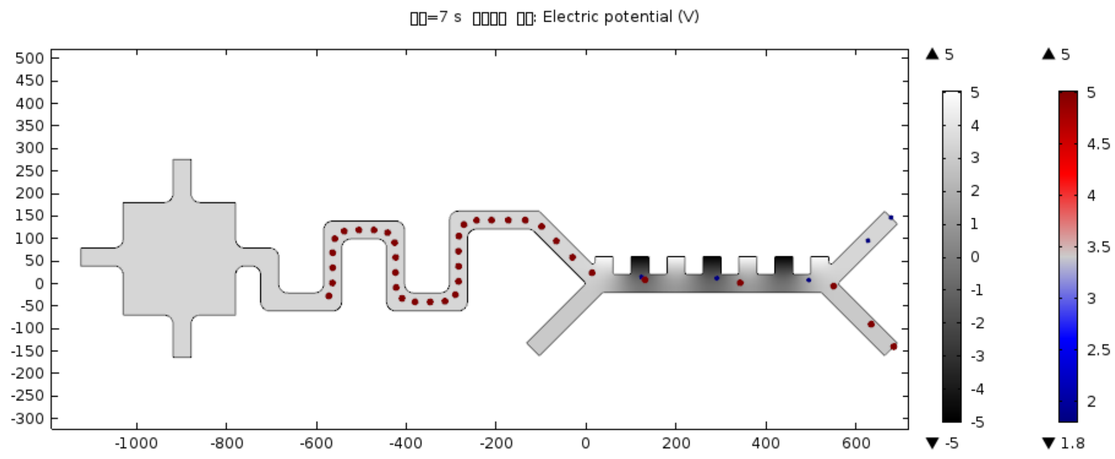


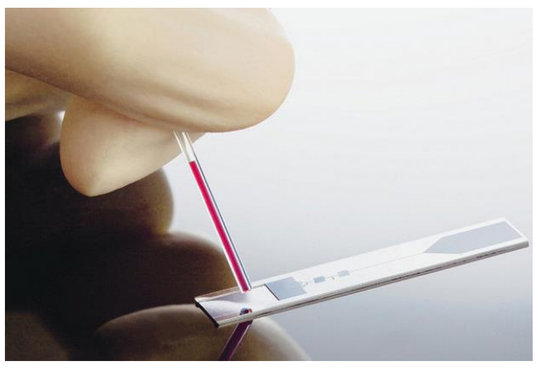
Figure 4: Particle Trajectories result in COMSOL simulation (t=7sec)

The blood sample and the chemical solutions have dynamic viscosities proportional to the concentration. As a result, the micropump can not pump too fast because it may cause too much turbulence and flow jam along microchannel. On the other hand, it can not pump too slow either, otherwise the testing time may be too long and the test result could also be degraded because the blood sample and chemical solutions may not be thoroughly mixed. Considering this, the micropump is set to work in periodic pumping mode. Its pressure P=sin(2*pi*f*t), where f is frequency (f=100Hz). The Reynolds number of the microfluid can be estimated as:

$$Re = \frac{\rho v D_H}{\mu} = \frac{v D_H}{\upsilon} = \frac{Q D_H}{\upsilon A}$$

where:
D_H is the hydraulic diameter of the pipe; L: characteristic travelled length (m).
Q is the volumetric flow rate (m^3/s).
A is the pipe cross-sectional area (m^2).
v is the mean velocity of the fluid (SI units: m/s).
μ is the dynamic viscosity of the fluid (Pa·s or N·s/m^2 or kg/(m·s)).
υ is the kinematic viscosity ($\upsilon = \mu / \rho$) (m^2/s); ρ is the density of the fluid (kg/m^3).
From the equation, we can see that Reynolds number is proportional to the travelled length and inversely proportional to the velocity of the fluid which is directly decided by the pump rate. Reynolds number can help us to estimate whether the microfluid is laminar or turbulent.

A Lab-on-a-Chip device developed by IBM Inc. is shown in the right figure. The goal of our research is to develop a low-cost bio-MEMS Lab-on-a-Chip device with size smaller than a credit card, which can be used to quickly diagnose disease by using a tiny drop of blood sample from the patient. Such lab-on-a-chip device will greatly improve the efficiency and resolution of disease diagnosis.



http://news.cnet.com/8301-13772_3-20012306-52.html

Conclusions and Future Work

Lab-on-a-chip device can handle sampling, reagent introduction, analysis and disease diagnosis using a single tiny MEMS chip. Such device can reduce reagent metering and protocol errors, reduce sample and reagent usage, and prevent contamination of the sample or infection of the user. In this poster, we proposed a complete bio-MEMS Lab-on-a-Chip device which integrates micropump, micromixer, microheater, dielectrophoresis and photodetector in a single chip. COMSOL simulation is used to verify the microfluid and particle behavior inside the device. The research will stay in upgrade. In the future, we will continue to improve the design, use COMSOL to simulate more processes in the chip, and eventually develop a device prototype for real sample testing.